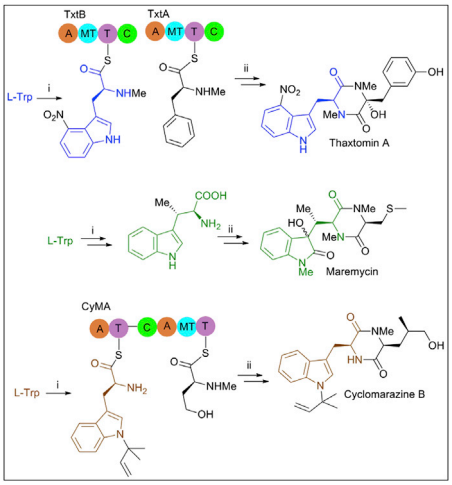
Chemistry & Biology

In This Issue

In Review: Biosynthetic Manipulation of Tryptophan in Bacteria

PAGE 317

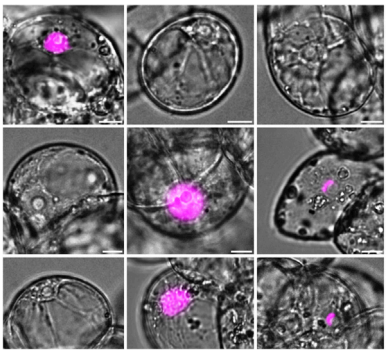
Tryptophan is a biosynthetic precursor to a large number of complex microbial natural products. Alkhalaf and Ryan review the pathways that enable incorporation of tryptophan into complex metabolites in bacteria.



In Brief: Converting Bacterial Toxin into Antibiotics

PAGE 329

Bacterial peptide toxins are well known mediators of pathogenicity. Solecki et al. show that a peptide toxin from *Staphylococcus aureus*, PepA1, has antibacterial activity and that it can be transformed from toxic to antibiotic derivatives. This suggests an innovative way to use bacterial toxins for good.



In Brief: Unlocking Alkaloids' Diversity in Madagascar Periwinkle

PAGE 336

How plants transform the central biosynthetic intermediate strictosidine into thousands of divergent alkaloids has remained unresolved. Stavrinides et al. discover a nuclear-localized alcohol dehydrogenase homolog responsible for conversion of strictosidine aglycone to tetrahydroalstonine that appears to interact with an upstream pathway enzyme.

Global View of *N*-Myristoylation in *Leishmania donovani*

PAGE 342

Wright et al. use metabolic tagging with an alkyne-myristate analog, click chemistry, and proteomics to identify lipidated proteins in two life stages of the parasite *Leishmania donovani*. Quantitative profiling of *N*-myristoyltransferase inhibition and identification of lipidation sites define the N-myristoylated proteome in this human pathogen.

From TrkB Agonist to Tackling Obesity in a Sex-Dependent Fashion

PAGE 355

Chan et al. find that consumption of the TrkB agonist 7,8-dihydroxyflavone (7,8-DHF) prevents the development of excess body weight gain though increasing the energy expenditure in skeletal muscle of female mice. The data reveal that the chronic activation of muscular TrkB by 7,8-DHF is useful in alleviating obesity in a sex-dependent fashion.

What's behind IAPP-Induced Cell Death and Bilayer Integrity Loss

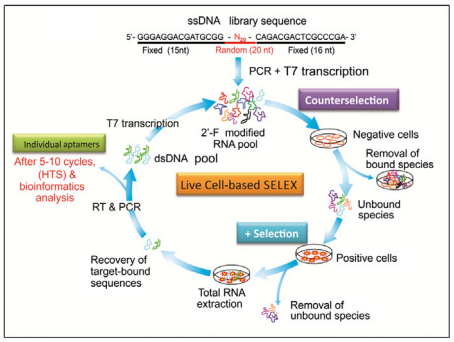
PAGE 369

A library of oligopyridylamide-based helical mimetics was designed and synthesized to target membrane-associated α-helical intermediates of islet amyloid polypeptide, a protein implicated in type II diabetes. Oligopyridylamides slow the rate of IAPP amyloid assembly and reduce membrane poration and toxicity in a rank order that links these functions.

Cell-Specific RNA Aptamer: A Double Agent

PAGE 379

Zhou et al. generated CCR5 RNA aptamers capable of specifically targeting HIV-1-susceptible cells (as siRNA delivery agent) and inhibiting HIV-1 infectivity (as antiviral agent) via block of the CCR5 required for HIV-1 to enter cells. Notably, this strategy can be utilized in disease models beyond HIV-1.



Inhibiting ATPase Activity of Hsp70 Suppresses Tumor Growth

PAGE 391

Ko et al. demonstrate that a small molecule, which inhibits an ATPase domain of Hsp70, induces caspase-dependent apoptosis by blocking interaction of Hsp70 with Apaf-1, without affecting interactions of Hsp70 with ASK1, JNK, Bax, and AIF. Animal model study shows that the small molecule suppresses tumor growth in mice.

Resource: Platform for a Streamlined Investigation of Proteasomes

PAGE 404

Intact protein mass spectrometry allows us to determine properties of protein complexes that are difficult to obtain through peptide-based methods. Gersch et al. introduce an analytical platform for the streamlined analysis of proteasome samples, revealing phosphorylation stoichiometries, inhibitor specificity, and sample heterogeneities.

Resource: Global View of Lipid Metabolism Regulation

PAGE 412

Casanovas et al. present a proteolipidomics platform for a comprehensive and quantitative time-resolved analysis of the yeast proteome and lipidome. Application of this platform demonstrates that lipid metabolism is regulated at the global scale and coordinated with remodeling of cellular architecture and processes during physiological adaptations.